

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Appln. of: Edwin Douglas Lephart et al.

Appln. No.: 10/533,045

Filed: October 20, 2005

For: USE OF EQUOL FOR  
TREATING ANDROGEN  
MEDIATED DISEASES

Attorney Docket No: 12957/20

Examiner: Zarek, Paul E.

Art Unit: 4161

Confirmation No. 6027

THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56 and §§1.97-1.98, and more particularly in accordance with 37 C.F.R. §1.97(b), Applicants hereby cite the following references:

OTHER ART

Aldercreutz, H., et al., "Urinary Excretion of Lignans and Isoflavonoid Phytoestrogens in Japanese Men and Women Consuming A Traditional Japanese Diet," *Am. J. Clin. Nutr.*, 54:1093-1100 (1991)

Axelson, M., et al., "The Identification of the Weak Oestrogen Equal [7-hydroxy-3'-4'-hydroxyphenyl]chroman] in Human Urine," *J. Biochem.*, 201:353-357 (1982)

Chang, Y.C., and Nair, M.G., "Metabolism of Daidzein and Genistein by Intestinal Bacteria," *J. of Natural Products*, 58(12):1892-1896 (1995)

Kurosawa, K., et al., "The Absolute Configurations of the Annual Metabolite, Equol, Three Naturally Occurring Isoflavans, and One Natural Isoflavanquinone," *Chemical Communications*, 1265-1264 (1968)

Magee, P., et al., "Equol: A Comparison of the Effects of the Racemic Compound with That of the Purified S-Enantiomer on the Growth, Invasion, and DNA Integrity of Breast and Prostate Cells In Vitro," *Nutrition and Cancer*, 54(2):232-242 (2006)

Marrian, G.F. and Haslewood, G.D., "CXLV. Equol, a New Inactive Phenol Isolated from the Keto-hydroxy-Oestrin Fraction of Mares' Urine," *University College, London, Department of Physiology and Biochemistry*, 1227-1232 (1932)

Muthyala, R.S., et al., "Equol, a Natural Estrogenic Metabolite from Soy Isoflavones: Convenient Preparation and Resolution of *R*- and *S*-equols and their Differing Binding and Biological Activity through Estrogen Receptors Alpha and Beta," *Bioorganic & Medicinal Chemistry*, 12:1559-1567 (2004)

Rowland, I.R., et al., "Interindividual Variation in Metabolism of Soy Isoflavones and Lignans: Influence of Habitual Diet on Equol Production by the Gut Microflora," *Nutrition and Cancer*, 36(1):27-32 (2000)

Setchell, K.D., et al., "S-Equol, A Potent Ligand for Estrogen Receptor  $\beta$ , is the Exclusive Enantiomeric form of the Soy Isoflavone Metabolite Produced by Human Intestinal Bacterial Flora," *Am. J. Clin. Nutr.*, 81:1072-1079 (2005)

Setchell, D.R. and Cole, S.J., "Method of Defining Equol-Producer Status and Its Frequency among Vegetarians," *J. of Nutrition*, 128:2188-2192 (2006)

Setchell, K.D., et al., "The Clinical Importance of the Metabolite Equol – A Clue to the Effectiveness of Soy and Its Isoflavones," *J. of Nutrition*, 132:3577-3584 (2002)

Setchell, K.D., et al., "Equol – Origins, Actions, and Clinical Relevance of this Specific Soy Isoflavone Metabolite," *Fifth International Symposium on the Role of Soy in Preventing and Treating Chronic Disease, Oral Presentation Abstracts, J. of Nutrition*, 134:1234S-1247S (2004)

Verbit, L. and Clark-Lewis, J.W., "Optically Active Aromatic Chromophores – VIII Studies in the Isoflavonoid and Rotenoid Serices," *Tetrahedron*, 24:5519-5527 (1968)

Wang, X.L., et al., "Enantioselective Synthesis of *S*-Equol from Dihydrodaidzein by a Newly Isolated Anaerobic Human Intestinal Bacterium," *Applied and Environmental Microbiology*, 71(1): 214-219 (2005)

Applicants also cite U.S. Pat. No. 7,396,855 issued on July 8, 2008 to Setchell et al.

Applicants are enclosing Form PTO-1449 (two sheets), along with a copy of each listed reference for which a copy is required under 37 C.F.R. §1.98(a)(2). As each of the listed references is in English, no further commentary is believed to be necessary.

37 C.F.R §1.98(a)(3). Applicants respectfully request the Examiner's consideration of the above references and entry thereof into the record of this application.

By submitting this Statement, Applicants are attempting to fully comply with the duty of candor and good faith mandated by 37 C.F.R. §1.56. As such, this Statement is not intended to constitute an admission that any of the enclosed references, or other information referred to therein, constitutes "prior art" or is otherwise "material to patentability," as that phrase is defined in 37 C.F.R. §1.56(a).

Applicants have calculated no fee to be due in connection with the filing of this Statement. However, the Director is authorized to charge any fee deficiency associated with the filing of this Statement to a deposit account, as authorized in the Transmittal accompanying this Statement.

Respectfully submitted,

February 10, 2009  
Date

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